United States
Environmental Protection
Agency

Office of Prevention,
Pesticides
and Toxic Substances
(7501C)

PESTICIDE FACT SHEET

Name of Chemical(s): Aminoethoxyvinylglycine

Reason for Issuance: Registration

Date Issued: April, 1997

Fact Sheet Number:

1. DESCRIPTION OF THE CHEMICAL

Generic Name(s) of the Active Ingredient(s):	Aminoethoxyvinylglycine (AVG), *L*-alpha-(2-aminoethoxyvinyl)glycine hydrochloride, or [S]-trans-2-amino-4-[2-aminoethoxy]-3-butanoic acid hydrochloride
OPP Chemical Codes	129104
Year of Initial Registration:	1997
Pesticide Type:	Biochemical plant regulator
U.S. and Foreign Producers:	Abbott Laboratories

2. USE SITES, APPLICATION TIMING & TARGET PESTS

Aminoethoxyvinylglycine (AVG) is a plant regulator, which in apples and pears reduces drops, may enhance fruit quality and firmness, and may, in apples, reduce the incidence of the physiological disorders water core and scald when applied in accordance with label directions. For certain ornamentals (miniature carnations, hibiscus, and rooted geranium cuttings and seedlings), the incidence of shipping-related problems such as flower senescence and flower bud abscission may be reduced.

Aminoethoxyvinylglycine is to be used as a spray solution, applied to apples or pears as a single application 28 days prior to the anticipated date of harvest, and to certain ornamentals 24 to 48 hours prior to boxing/shipping.

3. SCIENCE FINDINGS

A. TOXICOLOGY: All toxicity data requirements have been satisfied for the purpose of the conditional registration. The information submitted to support the acute toxicity requirements for AVG indicate toxicity category IV for acute oral toxicity, category III for acute dermal toxicity, category III for acute inhalation toxicity, category IV for primary eye irritation, and category IV for primary dermal irritation. Aminoethoxyvinylglycine is not a dermal sensitizer.

B. HUMAN HEALTH EFFECTS:

No unreasonable adverse effects to human health are expected from the use of AVG.

1. Risks Posed by Potential Dietary Exposure

Because the *Streptomyces* species that produces AVG is soil-born, the general population may be exposed to naturally-occurring AVG. The pesticidal use may, therefore, increase exposure above that from natural levels. Data from the currently submitted battery of acute toxicity/pathogenicity studies along with the associated time-limited tolerance is considered sufficient by the Agency to allow for a conclusion of no significant risk.

2. Effects on Immune and Endocrine Systems

The technical grade active ingredient caused immunosuppression in the rat. Absolute (49%) and relative (41%) thymus weights decreased significantly ($p \leq 0.05$) in the high dose group. The primary antibody response to sheep red blood cells (SRBC), measured by the mean number of anti-SRBC plaque-forming cells (PFCs) per spleen and per 10^6 viable spleen cells, decreased significantly ($p \leq 0.05$) at the end of the treatment period by 90% and 87%, respectively. The anti-SRBC response and thymus weight suppression was reversible in a 28-day recovery group of rats. Since the no observed effect level (NOEL) of 5 mg/kg/day in this study was higher than in the study used for RfD determination (1.77 mg/kg/day), the conclusions of no significant risk based on a 1000-fold safety factor for the proposed uses and exposure are not affected by the results of this study.

Available subchronic and developmental toxicity data do not indicate that AVG has any endocrine effects. EPA is currently in the process of determining how it will address estrogenic and thyroid effects from pesticide residues in general. Congress gave EPA two years to establish a screening and testing program for endocrine effects, and three years to implement the program. There is some information on estrogenic and thyroid effects from exposure to certain pesticides, but the data are limited. EPA is aware of data indicating adverse impacts

on animals, possibly involving endocrine disruption, from exposure to some environmental agents of human origin (i.e., PCBs). Although data are insufficient to warrant definitive statements on estrogenic effects or endocrine disruption by specific chemicals, the identification of the environmental agents which cause endocrine disruption and their mechanism of action will provide the Agency information for reducing risks, particularly to children.

3. Risks Posed by Potential Residential, School or Daycare Exposure

No residential, school or daycare uses currently appear on the labels. The use sites are all agricultural for use as a plant regulator on growing plants. Therefore, nondietary exposure to these sites where children are present is minimal to nonexistent.

4. Potential for the Transfer of the Pesticide to Drinking Water

In examining aggregate exposure, the Food Quality Protection Act (FQPA) directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

Because the Agency lacks sufficient water-related exposure data to complete a comprehensive drinking water risk assessment for many pesticides, EPA has commenced and nearly completed a process to identify a reasonable yet conservative bounding figure for the potential contribution of water-related exposure to the aggregate risk posed by a pesticide. In developing the bounding figure, EPA estimated residue levels in water for a number of specific pesticides using various data sources. The Agency then applied the estimated residue levels, in conjunction with appropriate toxicological endpoints (RfDs or acute dietary NOELs) and assumptions about body weight and consumption, to calculate, for each pesticide, the increment of aggregate risk contributed by consumption of contaminated water. While EPA has not yet pinpointed the appropriate bounding figure for consumption of contaminated water, the ranges the Agency is continuing to examine are all below the level that would cause AVG to exceed the RfD by the time-limited tolerances which have been granted for this pesticide. The Agency therefore concluded that the potential exposures associated with AVG in water, even at the higher levels the Agency is considering as a conservative upper bound, would not prevent the Agency from determining that there is a reasonable certainty of no harm, as required by FQPA.

5. Acute and Chronic Dietary Risks for Sensitive

Subpopulations, Particularly Infants and Children

Because the *Streptomyces* species that produces AVG is soil-born, the general population may be exposed to naturally-occurring AVG. The pesticidal use may, therefore, increase exposure above that from natural levels. Data from the currently submitted battery of acute toxicity/pathogenicity studies along with the associated time-limited tolerance is considered sufficient by the Agency to allow for a conclusion of no significant risk.

A dietary risk evaluation was performed using the RfD of 0.002 mg/kg/day and the Theoretical Maximum Residue Contribution (TMRC) as a worst-case scenario. The results from the Tolerance Assessment System Routine Chronic Analysis dated February 3, 1997 show:

Subpopulation:	Percent of RfD:
Nursing infants (<1 year old)	27.59
Non-nursing infants (<1 year old)	36.11
Children (1-6 years old)	11.19
Children (7-12 years old)	4.62
Males (13-19 years old)	2.12
Females (13-19 years old; non-pregnant, non-nursing)	2.11
Nursing females (13+ years old)	3.00
Pregnant females (13+ years old)	2.03

The percent of the RfD that will be utilized by the aggregate exposure to AVG will range from 4.6% for children 7-12 years old, up to 36.1% for non-nursing infants less than one year old. Because the RfD was based on a developmental study with a 1000-fold safety factor, infants potentially exposed at 36.1% RfD have an adequate margin of safety. Therefore, EPA concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure. A dietary risk evaluation based on Anticipated Residue Contribution (ARC) may indicate a lower dietary exposure to aminoethoxyvinylglycine.

6. Cumulative Exposure From Multiple Routes Including Dermal, Inhalation, and Oral

EPA does not have, at this time, available data to determine whether AVG has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, AVG does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that AVG has a common mechanism of toxicity with other substances.

Exposure to the agricultural-use end products will be primarily to mixer/loaders and applicators, occurring outdoors or in greenhouses. Exposure to others is expected to be minimal to nonexistent.

Skin and lungs would be the primary routes of exposure for mixers/loaders and applicators. In a 21-day repeated dose dermal toxicity study, the test compound caused no treatment-related signs of toxicity. No significant acute inhalation toxicity was observed in studies with the TGAI or the 15% end-use product. Thus, the risks anticipated for these routes of exposure are minimal. Oral exposure to AVG is possible through consumers eating treated produce.

Comparisons of the exposure estimates to the NOELs for maternal and developmental toxicity (using the value of 1.77 mg/kg/day for maternal and developmental toxicity), indicate unacceptable Margins of Exposure (MOEs) for mixer/loaders and airblast applicators wearing long pants, long-sleeved shirts and no gloves, and for greenhouse handgun applicators wearing long pants and long-sleeved shirts, with or without gloves.

These MOEs were calculated based on the most sensitive individual, a pregnant female, and thus the NOEL from the developmental toxicity study was used. However, the developmental toxicity study was based on oral exposure to the TGAI. The results of the 21-day repeated dose dermal toxicity study, in which no toxicity was observed at the highest dose tested (1000 mg a.i./kg/day), along with the results of the acute inhalation toxicity studies, mitigate concern over the dermal and inhalation risk of worker exposure to AVG.

End-use product labels require Personal Protection Equipment and a Restricted-Entry Interval of 12 hours to meet the Agency's Worker Protection Standard.

C. ECOLOGICAL EFFECTS:

AVG is practically nontoxic to freshwater fish and should not cause adverse effects to nontarget freshwater fish.

AVG is practically nontoxic to freshwater invertebrates and should not cause adverse effects in this species.

AVG is moderately toxic to northern bobwhite and may cause adverse effects if exposed to avian wildlife. Although the biochemical is naturally-occurring, the results of Tier I avian tests triggered the need for additional testing under current requirements for the proposed products. Abbott Laboratories responded to the need for data on environmental fate by submitting a terrestrial risk assessment. The data suggested that, when used in accordance with label directions, AVG is not expected to pose an unreasonable risk to avian species. However, due to the possible exception of grazing geese, mitigating label language will be employed. The additional label language is, "This pesticide is moderately toxic to avian species and exposure to birds should be avoided."

Risk to mammalian wildlife is expected to be minimal to nonexistent.

No significant toxicity to nontarget plants is expected from the use of AVG under the proposed use pattern.

The conditionally required nontarget insect or honeybee studies were not required for these products due to a limited possibility of exposure from the use pattern. However, the food-use end-product label must clearly state that application may occur only after fruit set.

It has been concluded from the data submitted that there would not be a "may affect" situation for endangered mammals, plants, insects and aquatic species from the proposed use of the products. Provided that the end-use product for use in apple and pear orchards is applied in accordance with its label directions, no unreasonable risk to endangered birds is expected.

4. Public Interest Finding

BPPD determined in the Public Interest Finding that conditional registration of an end-use product allowing application to apples would be in the public interest. Pears and ornamentals are minor crops which do not require analysis to qualify for a conditional registration.

BPPD reviewed the test information submitted by the registrant and concurred with the claim that application of AVG to apples would increase the quality of fruit at packout. A portion of the increased quality fruit would be marketed as fresh market apples instead of processed, and some would be of larger size or exhibit other quality improvements. These characteristics increase the market price to the grower, other things equal. However, a significant increase in the quantities of fresh market and higher grade apples would result in market price adjustments for apples where the consumer would obtain benefits in terms of lower price as well as more apples of higher quality. This means the grower, and possibly Abbott Laboratories, would receive lower monetary returns than projected by Abbott Laboratories.

5. SUMMARY OF DATA GAPS

Within four years (prior to the April 1, 2001 revocation/expiration date), a two-generation reproduction study (rat) is to be conducted and submitted for review. Also within four years, the submitted enforcement method must be validated by an EPA laboratory.

6. Regulatory Actions

A time-limited tolerance of 0.08 parts per million for residues of the biochemical plant regulator AVG in or on apples and pears was approved by the Director of the Office of Pesticide Programs on April 24, 1997. The first, conditional, registrations were issued on April 28, 1997.

7. CONTACT PERSON AT EPA **OFFICE LOCATION/TELEPHONE NUMBER**

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